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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SEHARASEYON, JEGATHEESAN	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 01/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/972,970	SHI ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/21/2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2, 12, 13 and 23-42* is/are pending in the application.

4a) Of the above claim(s) *2, 12 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This office action is response to Applicant's election of Group I, claims 23-42 (newly added claims) drawn to nucleic acid encoding a protein. Applicant also elects polynucleotides encoding SEQ ID NO: 4, including SEQ ID NO: 2. Election was made with traverse in the response filed on 10/21/03. The traversal is on the ground(s) that the Examiner has not shown that a "serious burden" would be imposed to search and examine these groups. Applicant asserts that with respect to a given sequence, a search of claims directed to that to that sequence would also provide useful information for the claims of the other groups directed to that sequence. This is not found to be persuasive because a search directed to a nucleotide sequence will not automatically lead to the identification of the antibodies directed to the protein encoded by such nucleotide. In addition, a search of this nucleotides will not result in the identification of the treatment methods using the nucleotide. Therefore, the searches for each of the groups are not coextensive and would be a burden on the Office to search all of the different claims of the groups or the various sequences. Therefore, the restriction requirement is deemed proper and made FINAL. Claims 2, 12 and 13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in response submitted on 10/21/03.

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

3. The disclosure is objected to because of the following informalities: The specification identifies the nucleotide sequence, amino acid sequence, plasmid cDNA and ATCC deposit by various alphabets (V, X, Y and Z). Applicant is required to provide the appropriate numerical number identifiers. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 30,31, 40 and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4a. Claims 30,31, 40 and 41 are rejected as vague and indefinite because the claims are directed to recombinant host cells, which could also read on a whole animal. Reciting that the host cells are "isolated" can obviate this rejection.

5.The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 33 is rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The plasmid HOFOB55 recited in claim 33 is essential to the claimed invention. It does not appear that the ordinary artisan can reproduce plasmid of the instant

invention. If the claimed cell lines are unique and cannot be produced by routine methods, deposit is required. If the deposit has been made under the terms of the Budapest Treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the cell line has been deposited under the Budapest Treaty and that the cell line will be irrevocably and without restriction or condition be released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample or for the enforceable life of the patent, whichever is longer. See 37 CFR 1.806. If the deposit has not been made under the Budapest treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature must be made, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met.

Applicant is required to state that the cell line has been deposited under the Budapest Treaty and that the cell line will be irrevocably and without restriction or condition be released to the public upon the issuance of a patent. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample or for the enforceable life of the patent, whichever is longer. Applicant's attention is directed to *In*

re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985), and 37 CFR 1.801-1.809 for further information concerning deposit practice.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6a. Claims 22-43 are rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific, substantial and credible utility. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose the biological role of the nucleic acid, the encoded protein, or the significance either.

It is clear from the instant specification that the "TM4SF" protein (SEQ ID NO: 4) described therein is what is termed an "orphan protein" in the art. This is a protein whose cDNA has been isolated because of its similarity to known proteins. There is little doubt that, after complete characterization, this protein and the nucleic acid encoding it, may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the

chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to nucleic acids and the protein encoded by the nucleic acid of as yet undetermined function or biological significance. There is absolutely no evidence of record or any line of reasoning that would support a conclusion that the "TM4SF" protein or the antibody binding to the "TM4SF" polypeptide of the instant application could be used in a method of diagnosing, treating, preventing, and/or prognosing disorders related to these TM4SF polypeptides, such as "immune disorders" (see paragraph 0423-0496 of the specification), "blood related disorders" (see paragraph 0497-0520 of the specification), "hyperproliferative disorder" (see paragraph 0521-0562 of the specification), "cardiovascular disorder" (see paragraph 0563-0577 of the specification), "respiratory disorders" (see paragraph 0578-0581 of the specification), "anti-angiogenesis related disorders" (see paragraph 0582-0607 of the specification), "cellular level diseases" (see paragraph 0608-0612 of the

specification), "wound healing and epithelial cell proliferation related disorders" (see paragraph 0613-0621 of the specification), "neurological disorders" (see paragraph 0622-0639 of the specification), "endocrine disorders" (see paragraph 0640-0652 of the specification), "reproductive disorders" (see paragraph 0653-0667 of the specification), "infectious diseases" (see paragraph 0668-0673 of the specification), "regeneration" (see paragraph 0674-0678 of the specification) and "gastrointestinal disorders" (see paragraph 0679-0687 of the specification). Neither the specification nor the prior art demonstrates a causal correlation or nexus of the claimed polypeptide with any of the plethora of conditions or disorders contemplated by the instant specification, therefore, there is no evidence of record that would provide for a method of treating, preventing or diagnosing any of the listed conditions or disorders. There is absolutely no evidence of record or any line of reasoning that would support a conclusion that the "TM4SF" protein of the instant application is involved in biological activities associated with signal transduction events and pathways, as well as cell motility, proliferation and metastasis. It is also suggested that a subset of the members of the TM4SF may function as potassium channel molecules. The record fails to indicate any evidence of any of these biological activities, and it would appear that until some actual and specific significance can be attributed to the protein identified in the specification as TM4SF, the gene encoding it, or the antibody that binds it, the instant invention is incomplete. The specification asserts that the claimed protein will have some activities similar to other TM4SF or F-box proteins

based on amino acid sequence similarity, but it is not clear or predictive which activity of the TM4SF or F-box family will be possessed by the claimed protein based on structural similarity alone. The protein of the instant specification is a compound which is known to share some structural similarity to the TM4SF family of proteins which are known in the art to have biological significance in signal transduction events and pathways, but also include cell adhesion in platelets and other lymphocytic and non-lymphocytic cell lines, as well as cell motility, proliferation and metastasis (see paragraph 0004 of the specification). However, as indicated in Todd et al. (BBA. 1399: 101-104, 1998) and Maecker et al. (FASEB J. 11, 428-442, 1997), the TM4SF family is complex and diverse. Todd et al. describe six new members of tetraspanin (TM4SF) genes. Maecker et al. describe that TM4SF genes are involved in cell activation, proliferation, adhesion, motility, differentiation and cancer. As the prior clearly teaches there is no well-established utility for the TM4SF family because the biological activities for the members of the family are diverse and not all the members share a common function. The references teach that the complexity of the TM4SF family and the TM4SF -induced responses is reflected in the diversity and redundancy of the TM4SF receptors. Thus, it appears that even with substantial homology among TM4SF family members there is still considerable diversity in its biological functions.

In the absence of knowledge of the biological significance of instant "TM4SF", there is no immediately obvious patentable use for the disclosed

nucleic acids or the polypeptide encoded by the same. The disclosed protein (SEQ ID NO: 4) only shares approximately 70% amino acid sequence similarity/identity with the most closely related protein (Tspan-5, Todd et al.) of the prior art (see Appendix A). Based on this degree of sequence similarity, it is unlikely and unpredictable if the claimed protein will possess any one biological activity of the prior art such as cell activation, proliferation, adhesion, motility, differentiation and cancer. Furthermore, the prior art of record demonstrates that the biological function of the protein family to which the disclosed protein is said to be a member is so diverse, that one could not predict which biological activity is possessed by the disclosed protein based on structural similarity alone, especially since all the members share structural similarity, but not functional similarity. To employ the instant invention in any of the disclosed methods would clearly require first using it as the object of further research to determine in which methods it could be used, that has been determined by the courts to be a utility which, alone, does not support patentability. Since the instant specification does not disclose a specific and substantial "real world" use for the claimed invention, it is incomplete and, therefore, does not meet the requirements of 35 U.S.C. §101 as being useful.

The instant specification provides data on expression of the claimed cDNA in several tissues including liver, lung, ovary and breast libraries (see Table 4 of the specification). However, there is no comparison of the expression in normal and diseased tissues that can be utilized for the purpose of identifying diseases. Applicants also assert that the

tissue distribution of mRNA expression of polynucleotides of the present invention was determined, but no data is provided. In addition, the disclosed library identification of the cDNA clone (HOFOB55) provided in Table 4, does not provide a specific, substantial and credible utility for the claimed polypeptides, because there is no comparison between normal and disease tissue. Expression of the claimed cDNA in disease (tumor) alone does not establish a nexus between the claimed protein and cancer growth. The instant specification fails to teach that the claimed polypeptide is diagnostic for any specific disease, as it is apparently found in normal and diseased tissue. Therefore, in the absence of a nexus or correlation with a particular disease or cancer, the instant specification does not disclose a credible "real world" use for the claimed invention, it is incomplete and, therefore, does not meet the requirements of 35 U.S.C. §101 as being useful.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7a. Claims 23-42 are rejected under 35 U.S.C. §112, first paragraph, as failing to adequately teach how to use the instant invention for those reasons given above (6a) with regard to the rejection of these claims under 35 U.S.C. §101.

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

1. Maecker et al. The terasanin superfamily: molecular facilitators (1997), FASEB J., 11, pp 428-442.

2. Todd et al. Sequences and expression of six new members of the tetraspanin/TM4SF family (1998), BBA, 1399, pp 101-104.

9. No claims are allowable.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 703-305-1112. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 703-308-4623. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

JS

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER